Assessing the Financial Value of Patient Engagement: A Quantitative Approach from CTTI's Patient Groups and Clinical Trials Project

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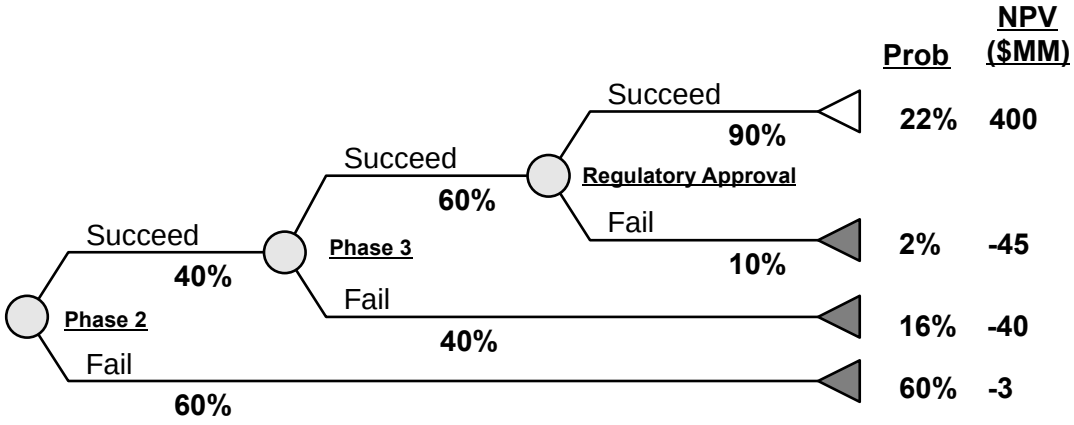
Supplement S1. Expected Net Present Value Model Details

Expected net present value (ENPV) is a common approach for valuing pharmaceutical and medical device development projects. The approach is to divide the future of the project into different paths toward conclusion, each associated with a probability the path will be taken and a present value of costs and revenues associated with that path.

As an example, consider the case of developing a drug for regulatory approval starting in phase 2 (**Figure S1**).

Figure S1. Example of a Simple ENPV Model for a Project in Phase 2[a]



[a]Circles represent uncertain events; values adjacent to each path from the circles indicate the probability that the project will follow that path. Values on the right indicate the probability that the project will terminate following that path and the NPV for that path (e.g., probability of technical and regulatory success = 22%). ENPV is calculated by totaling the product of the NPV and probability of each path. In this case, ENPV = (0.22 x $400) + (0.02 x -$45) + (0.16 x -$40) + (0.60 x -$3) = $77 MM.

The project may fail in phase 2, fail in phase 3, fail in regulatory approval or successfully launch. This is similar to the example used in the phase 2 base case. In the figure, failure in phase 2 is associated with a present value of failure of -$3 MM, meaning the company will lose $3 million in present value dollars. If phase 2 succeeds, the project advances to phase 3. Failure in phase 3 is associated with a present value of failure of -$40 MM. If phase 3 succeeds, the drug is submitted to a regulatory agency, which may approve or reject the submission. Rejection results in a loss $45 MM present day dollars, while success earns an NPV of $400 MM. In this manner, the several different paths of failure and one path of success for this drug are valued separately by present values of costs or revenue.

Technical risk is accounted for by the probability that the steps will succeed or fail. In the figure, phase 2 has a 40% chance of success, phase 3 has a 60% chance of success, and regulatory approval has a 90% chance of success. The probabilities can be estimated in numerous ways, including industry benchmarks, historical probabilities in a given company,

elicitations from structured interviews, or quantitative modeling. The probability of the four paths are calculated as the product of the probabilities of each step along that path. For example, the probability of succeeding in phase 2 and phase 3, but not getting approval (failure in the regulatory stage), is calculated as the product of 40% for succeeding in phase 2, 60% for succeeding in phase 3 and 10% of failing regulatory approval: 0.40 x 0.60 x 0.10 = 0.02, or 2%. The probability of succeeding in phase 2 and phase 3 and getting regulatory approval is 0.40 x 0.60 x 0.90 = 0.22, or 22%. The probabilities for each of the four paths are shown on the right in the figure.

Finally, ENPV is calculated by taking the value and probability of each path into account collectively. There is a 60% chance of losing $3MM in present day dollars, a 16% chance of losing $40MM, a 2% chance of losing $45MM and a 22% chance of earning $400 MM. The ENPV is the average present value considered over all four paths: ENPV = (0.22 x $400) + (0.02 x -$45) + (0.16 x -$40) + (0.60 x -$3) = $77 MM.

This ENPV indicates that, on average, the phase 2 project is expected to earn $77 million. Higher ENPVs indicate higher value projects. Lower ENPVs indicate lower value projects. Negative ENPVs indicate that the chances of failure are so great that they overwhelm the revenue from success.

Many real-world pharmaceutical projects are more complex than shown in the figure. ENPV models can be modified to accommodate different starting phases, multiple development paths to failure or success from a particular phase (e.g., early termination of studies due to safety concerns or an interim analysis; multiple indications studied in parallel), multiple definitions of success for the project overall (e.g., U.S. approval, E.U. approval or both), operational risk with different degrees of delay for each phase, and forecasting risk with multiple NPVs and

probabilities for each successful commercial outcome. More than two results (success, fail) from a study are also accommodated in ENPV models. These extensions complicate an ENPV model but do not change the general approach. For purposes of this paper, with no loss of generality of the methodology, we confine ourselves to single development path, single revenue stream, success/fail step examples as shown above.